Microfluidics: Rapid Mixing in Microfluidic Channels

Wyatt Vreeland (839) and Laurie Locascio (839)

This project deals with the use of bio-inspired vesicles for the spatial manipulation of specific species within a microfluidic environment. Central to microfluidic's implementation for integrated analysis is the ability to precisely control the spatial location of various species. Using a lipid vesicle (or liposome) to encapsulate a species of interest, allows species to be easily maneuvered through a microfluidic chip while being shielded from interactions with surrounding environment. When the species has reached its desired location in the microfluidic system, the liposome can be permeabilized releasing the intravesicular species into the microfluidic environment at a precise and controlled spatial location. Using this strategy we have demonstrated reagent mixing in distances approximately five times faster than standard passive mixing strategies

There were two major accomplishments associated with the project during the last fiscal year:

- *Use of liposomes for the rapid mixing of species*
- *Use of liposomes for spatially controlled reactions*

The liposome is a spherical structure composed of a phospholipid bilayer membrane that encapsulates a volume of intravesicular aqueous solution. Liposomes are bathed in an external aqueous solution and are generally ~100 nm to ~1 μm in diameter. The ability to encapsulate a species of interest inside liposomes renders that species inert to chemicals residing outside of the membrane. We have developed a bio-inspired liposome system that allows for the controlled introduction of polar species into a microfluidic system through the modulation of temperature using thermally triggerable liposomes. Thermally triggered liposomes take advantage of the dramatically increased bilayer permeability near the lipid chain melting transition temperature (T_m). Thus at a controlled temperature, a thermally triggerable liposome will release its contents into the extravesicular microfluidic space, allowing for precise delivery of agents to specific regions in the microfluidic environment.

The phenomenon is shown in Figure 1, where a solution of thermally triggerable liposomes (composition 97 % dipalmitoylphosphatidylcholine + 3% cholesterol) encapsulating self-quenched fluorescent sulforhodamine B flow through a microchannel with a lateral temperature gradient. The left end of the channel is thermostated at 20 °C and the right side is thermostated at temperatures ranging from 40 °C to 80 °C in 5 °C increments, please note that due to the low thermal conductivity of polycarbonate, the magnitude of temperature gradient in the channel is slightly less than the nominal temperatures at the termini. As the liposomes flow from the lower temperature region of the channel to the higher temperature region, they pass through the T_m that is specific for this formulation of liposomes (36 ˚C in this demonstration). At the T_m, the liposomes release the fluorescent dye into the extravesicular space causing an increase in fluorescence at that point and downstream in the channel in all panels except the first, where the temperature gradient does not pass through the T_m of this liposome formulation. Thus, the fluorescent dye, which was initially segregated from the

extravesicular space, is effectively “mixed” into the microfluidic environment. Because the liposomes are dispersed throughout the channel, mixing upon release from the liposomes is inherently quite fast. Measurement of the profiles in Figure 1 show the dye goes from “unmixed” to “mixed” state in approximately 200 μm under the experimental conditions shown here, whereas standard diffusive mixing would require almost 9 cm. Since this “mixing” technique is controlled by the T_m of the liposome formulation, rather than the fluid mechanical properties of the channel, this technique should be less sensitive to different operational flow rates than traditional microfabricated mixers. Additionally, because the liposome formulation dictates the T_m, mixed populations of liposomes can be used to control a series of sequential reactions where the temperature in the channel determines reaction timing and sequence.

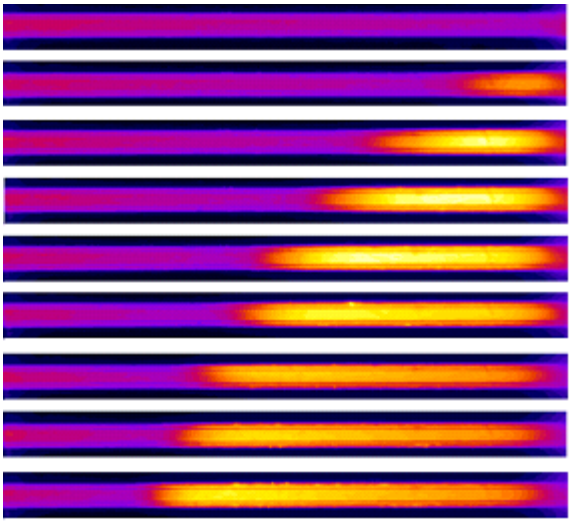

Figure 1. False-color micrographs of the fluorescence intensity of a solution of 97 mol% DPPC, 3 mol% cholesterol liposomes encapsulating self-quenched 100 mM sulforhodamine B in 0.5 M Tris buffer flowing through a polycarbonate microfluidic channel under different applied temperature gradients of 20°C-40°C to 40°C-80°C over 2 mm distance at a flow rate of 5 μL / hour